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THE TYPES OF HEMOLYTIC STREPTOCOCCI FOUND IN SCARLET FEVER PATIENTS AND IN THROATS OF GRAMMAR-SCHOOL CHILDREN¹



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Since the classical description of the disease by Sydenham, scarlet fever has been one of the chief causes of morbidity in the countries of the temperate zones. Administrative control of the disease has undergone marked changes, running from a long quarantine period, terminated only after completion of desquamation, to an arbitrary time limit of relatively short duration. Hospitalization of all cases has been attempted in certain English cities, while, in this country, attempts have been made to hospitalize a majority of the cases. In the face of these practices, the morbidity rate for scarlet fever has shown no definite downward trend, although the fatality rate has declined during the past 20 years.

Until the epidemiology of cholera and, to a less extent, diphtheria was understood, the administrative practices for the control of these diseases were of no avail in decreasing the morbidity from them.

In the case of scarlet fever much remains to be discovered as to its epidemiology, particularly, in the endemic cases. The majority of scarlet fever

cases occurring in a given locality cannot be directly traced, in most instances, to a known case of the disease.

Scarlet fever is not highly contagious. Casual exposure, therefore, to the disease does not imply that a given exposure was the infecting one in a given case. The wide distribution of hemolytic streptococci in the nasopharynx of the population, especially children, and the question of pathogenicity and specificity of such hemolytic streptococci, act as deterrents to epidemiological investigations of endemic scarlet fever. If the streptococci found in the throats of the population not obviously ill are non-pathogenic, they are of no significance; if these organisms are incapable of causing scarlet fever, they are of no importance in the epidemiology of that disease. If, on the other hand, these organisms be capable of causing scarlet fever, their importance might be very great.

The specificity of the hemolytic streptococci in relation to the diseases they cause has not been conclusively proven, although there is ample evidence that there are strains of that organism showing marked tendencies to cause specific diseases. Among these strains there are, undoubtedly, differences in virulence and invasive power and, in the case of the so-called scarlet fever streptococci, quantitative differences in toxin production. Whether or not a given hemolytic streptococcus can cause scarlet fever is not readily determined; depending as it does on the production by that organism

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of a toxin that can be neutralized by specific antitoxin. However, a method exists for the determination of toxigenicity. Also, there are methods whereby the hemolytic streptococci may be classified as to serological types (1). By utilizing serological classification and toxin production, it should be possible to collect data that might shed light on the epidemiology of scarlet fever.

METHODS AND MATERIAL

The work here reported was done to determine what types of hemolytic streptococci are found in scarlet fever patients in Chicago and to determine which of the types of that organism are found in the throats of grammar school children in the same region, in an attempt to show a bacteriological relationship between these two groups.

The scarlet fever patients used in this study were patients admitted to the Municipal Contagious Disease Hospital during the fall and winter of 1934 to 1935. There was no choice of patients, those admitted to one floor of the hospital being used; a total of 243 cases being studied.

For the school-child cultures the entire enrollment of three schools (710 children) was chosen: McKinley school (one of four schools in Moline) and the schools of Plano and Mt. Morris. All these towns are in Illinois. The choice of these schools was fortuitous but a happy one, as the Moline school was experiencing an epidemic of scarlet fever, the Mt. Morris school had had an epidemic the year previous, while there had been no scarlet fever in the Plano school.

Nose and throat cultures were made by swabbing the tonsils or tonsillar fauces with a dry, sterile, cotton swab and then using a second similar swab in the nose, reaching as far back as possible. In examining school children,

only throat cultures were made. Blood agar plates were inoculated by rubbing both swabs over approximately 4 centimeters of the media at the periphery of the plate. In the laboratory the plates were streaked with a wire, incubated 24 hours and examined. The medium used in these cultures was a meat-extract agar base, to which had been added about 5 per cent defibrinated sheep's blood.

Whenever possible, two beta hemolytic streptococcus colonies were picked and sown into a beef-infusion phosphate broth containing 1 per cent neopeptone. Cultures were stored in similar broth, to which defibrinated blood had been added. The cultures were sealed by the addition of about 2 cc of sterile paraffin oil.

Toxins were made by sowing a 24-hour broth culture of the streptococcus to be tested into 250 cc of beef-infusion, neopeptone broth adjusted to a pH of 7.8. After 3 days incubation at 37° C the broth was centrifuged and the supernatant filtered through an N Berkefeldt filter. The filtrate was then chilled and concentrated according to Veldee's (2) acetone precipitation method.

The toxins prepared as above were tested for potency by injecting 0.1 cc of a 1:1000 dilution intradermally on the ears of Dick-positive white rabbits.

All the toxins proven to be toxic by the above test were then tested for specificity. This was done by preparing pools of toxins, each pool containing equal parts of four toxins. These pools were then neutralized with Dick antitoxin and 0.2 cc of the neutralized material injected intradermally on the ears of another lot of Dick-positive white rabbits.

Two hundred and forty three cases of scarlet fever were studied as to the type of hemolytic streptococci present in their noses or throats or both. Table 1 shows

the types of hemolytic streptococci found on admission to the hospital.

the types encountered in these individuals.

TABLE 1
Types of hemolytic streptococci present on admission

Type	Number	Per cent	Probable error*
1	6	2.5	
2	52	21.4	±1.8
3	61	25.1	±1.9
4	2	0.8	
6	53	23.8	±1.8
Subtotal	179	73.6	±2.2
7	10	4.1	±0.8
8	6	2.5	
9	1	0.4	
10	2	0.8	
11	4	1.6	
12	1	0.4	
14	9	3.7	
15	3	1.2	
18	1	0.4	
Mixed	21	8.6	±1.2
Heterologous	6	2.5	
Total	243	100.0	

* In this report probable errors have been calculated only in those instances in which the number of the cases warrants it.

RESULTS

Cultures from cases

It will be seen that approximately three-fourths of the cases studied were caused by Griffith's types 1, 2, 3, 4 or 6, if we disregard those admitted with mixed infections; no other one type was responsible for more than 4 per cent of the cases. Excluding those types usually associated with scarlet fever, Griffith's type 7 caused more scarlet fever in this series than any of the other types.

Those individuals harboring two types of hemolytic streptococci were classified as mixed. Table 2 gives an analysis of

TABLE 2
Types of hemolytic streptococci encountered in mixed infections

Types	Number
3+6.....	6
2+6.....	2
2+3.....	1
2+other*.....	2
3+other.....	4
6+other.....	5
Wholly other.....	1

* By other is meant any type other than 1, 2, 3, 4 or 6; in other words, a type not frequently found in scarlet fever.

It is at once apparent that the figures showing the incidence of the frequently occurring types are too low because, of the twenty-one mixed infections, twenty of the individuals were infected with types 2, 3 or 6, while only one person with a mixed infection did not show a common scarlet fever type of streptococcus. In fact, almost one-half (nine) of the mixed infections were caused wholly by types 2, 3 or 6. Thus, in reality, 81.9 per cent of the cases harbored types 1, 2, 3, 4 or 6.

The question naturally arises as to whether or not any specific type of hemolytic streptococci is more virulent or more likely to cause complications than another.

One hundred and ninety seven of the 243 cases typed on admission, were, therefore, classified as to the presence or absence of complications at the time of admission (table 3).

Considering now only the three commonly occurring types, since they are the only ones that occur in sufficient numbers to be of any value, we find that type 2 appears in the complicated cases with about the same frequency as in the uncomplicated cases, while type 3 oc-

TABLE 3
Cases according to condition

Uncomplicated			Complicated		
Type	Number	Per cent	Type	Number	Per cent
1	3	2.5	1	1	0.5
2	21	10.6	2	18	9.1
3	43	21.8	3	17	9.0
6	30	15.2	4	1	0.5
7	1	0.5	6	20	10.5
8	3	2.5	7	1	0.5
9	1	0.5	11	1	0.5
10	1	0.5	12	1	0.5
11	2	1.0	Mixed	6	3.0
14	3	2.5	Het.	4	2.0
15	2	1.0			
Mixed	15	7.6			
Het.	1	0.5			
Total	126		Total	71	

curs a little more than twice as frequently in the uncomplicated cases as in those suffering a complication; type 6 occurs one and one-half times as often in the uncomplicated as in the complicated. Is this a true picture of the situation? To answer this question the cases uncomplicated on admission were further classified into two groups: those that remained uncomplicated during their hospitalization and those that developed complications after their admission to the hospital.

Of the 21 uncomplicated type 2 cases on admission, one third became complicated during their stay in the hospital; approximately one-third of the type 3 cases developed complications; and slightly more than one-fourth of the type 6 cases became complicated during hospitalization (table 4). If we now combine the cases complicated on admission with those developing complications after entering the hospital (table 5), we find that the incidence of complications among the three common groups is about the same; i.e., 64.1, 53.3, and

54.0 per cent for types 2, 3 and 6, respectively.

TABLE 4
Uncomplicated cases during hospitalization

Type	Uncomplicated	Became complicated	Remained uncomplicated
1	3	0	3
2	21	7	14
3	43	15	28
6	30	7	23
7	1	1	0
8	3	1	2
9	1	0	1
10	1	0	1
11	2	0	2
14	3	0	3
15	2	0	2
Mixed	15	1	14
Het.	1	0	1
Total	126	32	94

TABLE 5
Uncomplicated and complicated cases by types of streptococci

Type	Total cases	Total cases complicated	Per cent complicated	Probable error
1	4	1	25.0	
2	39	25	64.1	± 5.2
3	60	32	53.3	± 4.3
4	1	1	100.0	
6	50	27	54.0	± 4.8
7	2	2	100.0	
8	3	1	33.3	
11	1	1	100.0	
12	1	1	100.0	
18	1	1	100.0	
Mixed	21	7	33.3	
Het.	5	4	80.0	
Total	197	103	52.3	

The higher incidence of complications in type 2 cases may be due to the small number of cases in that group. Whether complications or death rate is the more reliable guide to severity of infection is an open question. If, however, fatality

be considered as a guide to severity, type 2 is certainly the most virulent of the streptococci concerned with this epidemic. Of the 243 cases types, five died; of these, four were type 2 infections. The other death occurred in a butcher suffering from a surgical scarlet fever contracted from abrasions and cuts on his hands. He died 3 days after admission, from a septicemia, diagnosed by blood culture, caused by a type 15 streptococcus.

Gunn and Griffith (3), as well as Smith (4), believe that the complications developing late in the course of the disease are caused by the patient's becoming reinfected with a different type of streptococcus contracted from another patient in the ward. This is an interesting explanation for complications but needs more proof than has been advanced before it can be accepted. To test this theory, 161 cases were cultured and typed 1 day before discharge from the hospital. As in cases examined at the time of admission, types 2, 3 and 6 were found most frequently. These three types composed 77.6 per cent of all cases typed on dismissal. It will be noted that in the "admission cultures"

TABLE 6
Types present on discharge

Type	Number	Per cent	Probable error
1	1	0.6	
2	41	25.5	± 2.3
3	25	15.5	± 1.9
6	59	36.6	± 2.6
7	2	1.2	
8	8	5.0	
14	1	0.6	
15	2	1.2	
18	1	0.6	
Mixed	16	9.9	
Het.	5	3.1	
Total	161	100.0	

TABLE 7
Change in type

Type on admission	Type on discharge	Number	Per cent
2	2	16	61.5
2	3	3	11.5
2	6	3	11.5
2	1	1	3.8
2	15	1	3.8
2	Mixed	2	7.7
Total		26	
3	3	12	29.3
3	2	6	14.6
3	6	15	37.2
3	8	2	4.9
3	Mixed	4	9.7
3	Het.	2	4.9
Total		41	
6	6	20	58.8
6	3	1	2.9
6	2	5	14.7
6	7	1	2.9
6	8	2	5.9
6	Mixed	3	8.8
6	Het.	2	5.9
Total		34	

the incidence of the three main types is fairly equal while in the dismissal cultures, there is considerable variation among the three types (table 6).

Type 2 had about the same incidence as in the admission cultures, while type 3 showed the lowest incidence in the dismissal cultures. Type 6 is the most frequent on discharge.

Among the 161 "discharge cultures," 101 had been of types 2, 3 or 6 upon admission. Table 7 shows the admission and discharge cultures of these 101 cases.

The same organism was present in forty-eight instances in the nose or throat of these individuals. In individuals admitted with type 2 infections, 61.5 per cent harbored the same type

upon dismissal; in those admitted with type 6, 58.8 per cent showed the same type upon dismissal; while of the 41 type 3 infections, only 12 (29.3 per cent) had the same type on leaving the hospital. This points toward the possible existence of an inherent ability of the streptococci to change type while in the host, apparently most pronounced in type 3. Accordingly, an analysis of the cases was made for the presence or absence of complications in the light of their cultures on admission and discharge from the hospital (table 8).

TABLE 8

Change in type in uncomplicated and complicated cases

On admission		At discharge						
Type of strep.	Number of cases	Type						
		2	3	6	Other	Mixed	Het.	Per cent change
Uncomplicated:								
2	12	8	1	3	0	0	0	4
3	23	4	5	10	0	4	0	18
6	19	5	1	10	0	2	1	9
Total	54	17	7	23	0	6	1	57.4
Complicated in hospital:								
2	4	2	2	0	0	0	0	2
3	9	2	4	2	0	1	0	5
6	5	0	0	3	1	0	1	2
Total	18	4	6	5	1	1	1	50.0

We find that of 54 patients admitted "uncomplicated" and remaining so, 31 (57.6 per cent), left the hospital with a type of streptococcus different from that which they harbored on admission; while, in the group developing complications in the hospital, 9 (50 per cent) were dismissed with a different type of streptococcus in their nose and throat.

Cultures from school children

A total of 710 school children was cultured. Of the 231 cultures made in Moline, 78 (33.8 per cent) contained hemolytic streptococci. In the Plano school 254 cultures were made, of which 65 (25.6 per cent) contained hemolytic streptococci while, in Mt. Morris, about the same results were obtained; that is, 30.6 per cent of the 225 cultures showed hemolytic streptococci. Table 9 shows the distribution of carriers in the various grades in these schools. The carrier rate in the Moline school is not significantly higher than that in Plano and Mt. Morris where no scarlet fever existed.

TABLE 9

Distribution of carriers by grades and sex in three grammar schools

School	Grade	Children examined			Positive for hemolytic streptococci				
		Boys	Girls	Total	Boys	Girls	Total	Per cent	Probable error
Moline	Kindg.	2	6	8	0	3	3		
	First	11	14	25	4	4	8		
	Second	6	15	21	3	5	8		
	Third	20	15	35	8	8	16		
	Fourth	15	19	34	9	5	14		
	Fifth	13	11	24	3	4	7		
	Sixth	16	7	23	5	3	8		
	Seventh	13	13	26	7	1	8		
	Eighth	12	23	35	5	1	6		
	Total			231			78	33.8	±2.1
Plano	First	17	16	33	4	2	6		
	Second	10	19	29	5	3	8		
	Third	23	12	35	12	6	18		
	Fourth	15	16	31	4	2	6		
	Fifth	23	16	39	3	4	7		
	Sixth	15	14	29	3	4	7		
	Seventh	15	15	30	3	4	7		
	Eighth	12	16	28	3	3	6		
	Total			254			65	25.6	±1.8
Mt. Morris	First	20	17	37	10	5	15		
	Second	11	10	21	4	4	8		
	Third	14	8	22	7	3	10		
	Fourth	12	14	26	6	5	11		
	Fifth	19	17	36	6	3	9		
	Sixth	16	9	25	3	3	6		
	Seventh	13	15	28	3	2	5		
	Eighth	17	13	30	2	3	5		
	Total			225			69	30.6	±2.1
Grand total.....				710			212	29.8	±1.4

In the case of Mt. Morris and Plano, at least, the legitimate question arises:

how many of these cultures are scarlet fever streptococci? While the same question might be asked regarding Moline, epidemiological evidence points strongly to the fact that the carriers in that school were harboring scarlet fever streptococci, although there is no absolute proof. A total of 243 cultures was examined for type, and 91 per cent were found to be of those types most frequently found in scarlet fever.

There is little difference in the total incidence of the scarlet fever types in the three schools, although the incidence of each specific type varies markedly in each (table 10).

TABLE 10

Types of hemolytic streptococci found in children of three grammar schools

Type	Moline	Plano	Mt. Morris	Total	Per cent	Probable error
1	36	13	10	59	24.2	±1.8
2	4	21	1	26	10.7	±1.3
3	11	5	0	16	6.5	±1.1
4	1	17	5	23	9.5	±1.3
6	41	29	14	84	34.6	±2.0
7	0	3	1	4	1.6	
8	3	2	2	7	2.9	
10	0	1	0	1	0.4	
14	0	0	1	1	0.4	
15	0	1	0	1	0.4	
Het.	2	12	0	14	5.8	±1.0
Untyped	1	4	2	7	2.9	
Total	99	108	36	243	100.0	

It is possible, of course, that these scarlet fever types of streptococci exist in a non-toxigenic state in the nasopharynx of the healthy vector and are, therefore, without significance. To test this possibility, 183 of the cultures from these three schools were examined for toxin production.

Of the 183 toxins tested, 161 (87.9 per cent) proved to be toxic. Of these 161 toxin-producing strains, 30 (16.4 per

cent) produced toxins giving less intense reactions than did the others.

These toxins were concentrated ten times and, if one assumes that the treatment did not reduce the toxicity, one may well reason that the weakly toxic strains should be regarded as negative. On this basis, 131 (71.6 per cent) of the 183 strains tested were toxic. These 131 toxic strains were fairly equally distributed among the three schools, as shown in table 11.

TABLE 11

Toxicity of strains found in three grammar schools

	Strains tested	Strains highly toxic	Per cent highly toxic	Probable error
Moline.....	52	39	75.0	±4.0
Plano.....	90	67	74.4	±3.1
Mt. Morris..	41	25	60.9	±5.1
Total.....	183	131	71.6	±2.2

It is of interest that, in Moline, where scarlet fever was epidemic, the number of cultures proven to be toxic was but 5 per cent greater than in the two non-infected schools.

It must be remembered that the above figures are for all toxic cultures regardless of type of hemolytic streptococci, which brings up the question as to whether or not the types of hemolytic streptococci most frequently encountered in scarlet fever present any difference in toxin production as compared with those less frequently found in the disease. Table 12 shows that they do not.

Among 142 cultures of the types usually encountered in scarlet fever, there were 38 (26.7 per cent) that produced weak toxin or none at all; while 11 (26.8 per cent) of the 41 cultures of less frequently occurring types were non-toxic or but weakly toxigenic. These numbers are small; a fact which must

TABLE 12

Toxin production by 142 strains of scarlet fever streptococci

Type	Potent	Weak	Negative	Total	Per cent negative
1	25	8	6	39	15.4
2	14	3	1	18	5.5
3	7	1	1	9	11.1
4	15	3	5	23	21.7
6	43	8	2	53	3.8
Total	104	23	15	142	10.6

be borne in mind in drawing conclusions. This is especially true of the group not frequently causing scarlet fever. These types, however, apparently are infrequently found, so that the small numbers are probably not as significant as they would be if these organisms were commonly encountered.

So far as the individual schools are concerned, the numbers of cultures from each are too small to be of any significance although, in Moline during the epidemic, no frankly nontoxic strains were encountered and all the weak toxins were from strains frequently causing scarlet fever (table 13).

TABLE 13

Toxin production by hemolytic streptococci from children of three grammar schools

	Moline	Plano	Mt. Morris	Total	Per cent	Probable error
Cultures toxic.....	39	67	25	131	71.3	± 2.2
Cultures nontoxic	0	14	8	22	12.4	± 1.6
Cultures weakly toxic.....	13	9	8	30	16.3	± 1.8
Total.....	52	90	41	183	100.0	

The epidemiological importance of the toxin-producing hemolytic streptococci

is better shown if the carriers, rather than the cultures themselves, are studied.

Accordingly, cultures from 145 of the vectors were examined as to the types of hemolytic streptococci carried by them. Table 14 shows the distribution

TABLE 14

Individuals in three grammar schools harboring various types of hemolytic streptococci

	Vectors typed	Vectors of types 1 to 6	Vectors of other types	Per cent vectors types 1 to 6	Probable error
Moline....	53	51	2	96.2	± 5.6
Plano.....	64	59	5	92.2	± 2.2
Mt. Morris	28	25	3	90.0	± 12.1
Total.....	145	135	10	93.1	± 1.4

of carriers according to the types of hemolytic streptococci harbored by them. It is apparent that 93 per cent of the vectors of hemolytic streptococci harbor types frequently found in scarlet fever.

There is a remarkable uniformity in the distribution of the carriers of these types in the three schools. In fact, there is no significant difference among the three, although it is of interest that but 4 per cent of the vectors in the Moline school harbored hemolytic streptococci of a type infrequently found in scarlet fever.

Here again arises the question of toxin production by the strains carried. Of the above 145 cultures from vectors, 134 were examined for toxigenicity. Table 15 shows the distribution of vectors of toxic, weakly toxic, and nontoxic strains in the three schools. Of the 134 vectors studied, 109 harbored toxic strains and only ten were carriers of nontoxic strains. The remaining fifteen individuals were vectors of weakly toxigenic strains. Thus, 81.3 per cent of the vectors studied carried toxic strains;

TABLE 15
Toxigenicity of hemolytic streptococci carried by individuals in three grammar schools

	Mo-line	Plano	Mt. Morris	Total	Per cent	Probable error
Vectors of toxic strains . . .	37	50	22	109	81.4	±2.3
Vectors of nontoxic strains . . .	0	7	3	10	7.5	±4.3
Vectors of weakly-toxic strains . . .	10	3	2	15	11.1	±4.9
Total . . .	47	60	27	134	100.0	

11.1 per cent carried weakly toxic strains; and but 7.5 per cent carried frankly nontoxic strains of hemolytic streptococci.

DISCUSSION

These data from the scarlet fever cases shows clearly that, during the epidemic of 1934 to 1935, most of the cases were caused by three of the Griffith types; types 2, 3 and 6. While it is true that the number of cultures typed is small the rates for types 2, 3 and 6 are highly significant, as the probable error is approximately one-twelfth of the rate for types 2 and 6 and one-thirteenth the rate for type 3. The only other suggestive rates are for types 7 and 14 and these are barely significant. It is probably significant that the type 14 cultures were obtained early in the fall before the epidemic had assumed any considerable magnitude. The cases harboring type 7 are important from an epidemiological standpoint. This type was originally isolated by Griffith from a case of puerperal sepsis. Some obstetricians consider many cases of puerperal sepsis as surgical scarlet fever. In these type 7 cases is presented evidence, if it be

needed, that the organism capable of causing puerperal fever can, and does, cause scarlet fever. This same organism, in this country, frequently (according to Griffith) causes erysipelas. In this connection it should be mentioned that the grandmother of one of the children having scarlet fever caused by type 7 hemolytic streptococci was ill with erysipelas at the same time as the child. As the grandmother was being treated at another hospital it was impossible to determine the type of streptococci concerned with her erysipelas attack. Obviously, the mere fact that a child has scarlet fever at the same time that its grandmother has erysipelas does not mean that either of the individuals infected the other, but it is suggestive of the possibility that a relationship between the two diseases exists when one considers that the causative organism of the attack of scarlet fever was one which frequently causes erysipelas.

Another fact of epidemiological significance is the high incidence of type 6 infections in this series. In England this organism is frequently found in tonsillitis and sore throats and but very infrequently in scarlet fever. In this epidemic almost 24 per cent of the cases were caused by the "sore throat" type. If this type of hemolytic streptococcus is a sore throat type and yet causes almost one-fourth of the cases of scarlet fever studied, it is obvious that the sore throat is an important source of scarlet fever.

The question of virulence of an organism is difficult to determine unless death be used as a criterion. If the presence of complications be taken as a criterion, the subjective influence in determining what constitutes a complication tends to militate against an accurate appraisal of virulence. Obviously, the complications demonstrated by ob-

jective tests such as the presence of blood in urine or a discharging middle ear offer no difficulty, but the question of whether or not a cervical lymph gland has swollen to a size sufficient to warrant treatment is entirely one of judgment. In this series of cases, a case has been considered complicated when treatment for the complication had been ordered by the attending physician.

That there is no difference in the virulence of the three commonly occurring streptococci of this epidemic is amply demonstrated if the probable errors of the rates are considered. If we assume that the rate based upon the smallest number of cases is too high by the amount of its negative probable error and the others too low by the amount of their positive probable errors, we find the rates becoming 58.9 per cent, 57.6 per cent and 58.8 per cent for types 2, 3 and 6 respectively. Even if the converse be assumed the difference between the highest and the lowest rate would amount to approximately only 20 per cent.

It must be remembered that the number of cases yielding these data is small and, furthermore, cover only 1 year. Larger numbers of cases might change the data and it is conceivable that in another locality, in another year, the virulence of the types might undergo a change.

The development of complications late in the disease may or may not be due to the reinfection of the patient with a different type of hemolytic streptococcus. Were this the case one would expect, on the basis of logic alone, that cases treated in the home would seldom develop complications late in the course of the disease. The data concerning the types of streptococci present at the time the patients were discharged from the

hospital clearly show that the same types were found as on admission, but that the distribution of the main types had changed. If the presence of a new type is due to reinfection from another individual harboring the new type, all types should show about the same incidence in the dismissal cultures, since the three types were about equally divided on admission. Slightly more than 50 per cent of the uncomplicated cases left the hospital with a type of hemolytic streptococcus different from that causing their infection while, in the few cases developing complications during their hospitalization, one half showed a different type on dismissal.

If these groups be combined, we have 40 (55 per cent) of the 72 uncomplicated cases harboring, on discharge, a different type of streptococcus from that found on admission. Twenty-five per cent of the 72 cases became complicated during their hospitalization. If complications are due to the reinfection of the patient with a new type of streptococcus, one might expect the complication rate to approach 55 per cent. While the general complication rate among 197 patients is 36 ± 2.3 per cent, among the 72 cases showing a type of hemolytic streptococcus on discharge which was different from that causing the disease, the complication rate was 25 ± 3.4 per cent. From these figures it is apparent that the new streptococcus per se played a small rôle, if any, in the causation of complications. It must be mentioned, furthermore, that all these cases were treated in two-bed cubicles, the walls of which reached the floor, thus reducing the chance of reinfection with another type of streptococcus. It seems reasonable to infer, therefore, that the hemolytic streptococcus has the potentiality of changing its type through residence in an immune host. This ability

to change type is apparently most marked in type 3 and least in type 2, while type 6 holds an intermediate position among these three types. The small number of other types studied prevents any assumption regarding them.

The fact that slightly over 90 per cent of the streptococci isolated from the throats of grammar school children were of the types frequently found in scarlet fever may be of great importance in the epidemiology of that disease. It is possible that here, in these apparently well children, is the reservoir of endemic scarlet fever.

The fact that there was only a slight difference in the incidence of the types of streptococci frequently causing scarlet fever in the schools where no scarlet fever was occurring, and where it was epidemic, further strengthens the possibility that the healthy carrier acts as the reservoir of scarlet fever for, if the epidemic of scarlet fever was due to the introduction of streptococci frequently causing scarlet fever into the school, the rate of those streptococci should have been much higher than in the other schools.

The data clearly show that the hemolytic streptococci isolated from the throats of these school children produced toxin that could be neutralized by specific antitoxin. Thus, one may state that these toxic strains were streptococci capable of causing scarlet fever. It must be borne in mind, in connection with the toxigenicity of these streptococci, that the method used in concentrating and purifying the toxins reduces their potency. Rane (5) states a marked reduction in potency occurs with each acetone treatment given the toxin. On the other hand, these toxins were concentrated ten times so that it is possible that the concentration made up for the loss in potency due to purification.

When the toxigenicity of the types frequently causing scarlet fever is compared with the types less frequently doing so, one is struck by the fact that there is no difference between the two; approximately three-quarters of the cultures in each class produce strong toxins.

When the children, as carriers, are considered rather than the organisms they carry, the importance of the carrier condition becomes even more apparent. Only 7 per cent of the carriers studied harbored types not frequently causing scarlet fever. Of the vectors studied for toxin-producing strains, slightly more than three-fifths carried highly toxic strains and over 90 per cent harbored strains of some degree of potency.

The data herein presented show clearly that there is a close bacteriological relationship between the types of hemolytic streptococci frequently found in scarlet fever and those found in the throats of grammar-school children. The incidence of the various individual types varies from place to place, and might vary from year to year but, as a group, there is no difference between the types found in a general grammar-school population and those frequently causing scarlet fever.

CONCLUSIONS

The above-presented data allow the following conclusions to be drawn:

1. Griffith's types 2, 3 and 6 hemolytic streptococci were the types most frequently encountered in the cases studied during the scarlet fever epidemic in Chicago during 1934 to 1935.

2. No difference in virulence, on the basis of the presence of complications, could be detected between types 2, 3 and 6.

3. A small but appreciable number of cases of scarlet fever was caused by a

type of streptococcus frequently found in erysipelas.

4. The vector rate in a school where scarlet fever was epidemic was no higher than the rate where no scarlet fever was occurring.

5. There was no difference between the types of hemolytic streptococci found in schools where there was no scarlet fever and those found where it was epidemic.

6. The vectors of hemolytic streptococci harbored types of streptococci most frequently causing scarlet fever.

7. Approximately 90 per cent of the vectors harbored strains of hemolytic streptococci that produce toxin neutralized by scarlet fever antitoxin.

8. There is a direct bacteriological relationship between the grammar-school

children harboring hemolytic streptococci and cases of scarlet fever.

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